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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

FLUIDIGM CORPORATION, a Delaware
corporation; and FLUIDIGM CANADA INC.,
a foreign corporation,

Plaintiffs,

v.

IONPATH, INC., a Delaware corporation,

Defendant.

Case No. 3:19-cv-05639

**PLAINTIFF FLUIDIGM'S REPLY IN
SUPPORT OF CLAIM CONSTRUCTION**

TABLE OF CONTENTS

Table of Contents	i
Table of Authorities	ii
I. “Vaporizing, Atomizing, and Ionizing.”	2
A. There is No “Three-Step” Requirement, Much Less a Required Order of Steps.....	2
B. Neither the Claims Nor Patents Require “Heat.”	6
II. “Detection” of the Transient Signals of the Elemental Tags.	8
III. “Lanthanide or Noble Metal.”	10
IV. IONpath Seeks to Add an Entirely New Piece of Equipment to “First Device.”	11
V. The Claimed “Second Device” is a Mass Spectrometer.	12
VI. “Sequentially.”	13
VII. “Transient Signal.”	14
VIII. “Distinct Isotope.”	15
IX. “Pretreating”	15

TABLE OF AUTHORITIES

Cases

<i>Altiris, Inc. v. Symantec Corp.</i> , 318 F.3d 1363 (Fed. Cir. 2003)	4
<i>Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.</i> , 246 F.3d 1368 (Fed. Cir. 2001)	13
<i>GE Lighting Sols., LLC v. AgiLight, Inc.</i> , 750 F.3d 1304 (Fed. Cir. 2014)	7, 8
<i>Interactive Gift Exp., Inc. v. Compuserve Inc.</i> , 256 F.3d 1323 (Fed. Cir. 2001)	4
<i>Koninklijke Philips N.V. v. Zoll Med. Corp.</i> , 656 F. App'x 504 (Fed. Cir. 2016)	4
<i>Maxim Integrated Prod., Inc. v. Silicon Mitus Tech., Inc.</i> , No. 17-CV-03507 NC, 2018 WL 4657384 (N.D. Cal. July 3, 2018)	4
<i>SciMed Life Sys. Inc. v. Advanced Cardiovascular Sys., Inc.</i> , 242 F.3d 1337, 1341 (Fed. Cir. 2001)	7

Defendant IONpath’s Responsive Claim Construction Brief (ECF No. 113) (“Ip. Br.”) improperly attempts to add multiple features of particular embodiments, and even additional equipment, into the claims. In so doing, IONpath ignores and mischaracterizes the actual claim language, inventions, and intrinsic evidence of the Patents. Below are just some of the many errors IONpath invites:

1. IONpath’s proposed construction of “vaporizing, atomizing, and ionizing” adds a non-existent three-step sequential process that IONpath admits would also require adding two new transformative words to the claim. Ip. Br. at 5 (“an injected sample is ‘vaporized’ *then* ‘atomized’ and *finally* ‘ionized’ as it moves through the system” (emphasis added)). The claims at issue do not use these words and do not use the word “sequential” for this limitation as they are not applicable. Indeed, the inventors knew when and how to use “sequential” in the claims; they did so with respect to defining “detecting” as well as in the preamble. That the inventors knew how to describe a sequential process and chose not to with respect to “vaporizing, atomizing, and ionizing” alone should be dispositive.

2. IONpath’s argument that “vaporizing” is a “specific process that uses heat” finds no support in either the claims or specification. *Id.* at 6. The new term “heat” does not appear in the claims and would constitute the injection of a wholly-new limitation into the claims. IONpath’s admission that many types of glow discharge devices -- one of several “suitable devices” disclosed for “vaporizing, atomizing, and ionizing” -- do not use heat for vaporization alone requires the rejection of IONpath’s new “heating” limitation. *Id.* at 7.

3. IONpath inserts an unclaimed and *completely separate piece of equipment* (a cell or particle injection system) as part of “a first device to vaporize, atomize, and ionize multiple elemental tags.” *Id.* at 12. This additional equipment does not even perform the claimed “vaporizing, atomizing, and ionizing,” and the specification, appropriately, does not identify it in the list of “suitable devices” for performing this step. *See* ‘386 Patent (ECF No. 109-4), 6:59-64.

4. IONpath requires that “detect” must encompass the *entire* elemental composition of cells, although the plain language of the claim encompasses detecting *only* a transient signal of

the vaporized, atomized, and ionized lanthanide and noble metal elemental “tags.” Ip. Br. at 16.^{1/} As a result, IONpath’s construction requires the Court to not only insert the limitation “entire” into the claims, but also completely ignore the actual language of the claims. *See, e.g.*, ‘698 Patent (ECF No. 109-5), 30:66-31:3 (“... detect, by mass spectrometry, lanthanides and/or noble metals of the single first cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single first cell ...”).

5. IONpath also asks the Court to entirely divorce the fundamental temporal meaning of “sequentially” from “*detected sequentially*” such that there is no “timing” requirement and, instead, redefines the word to require discerning the *entire* elemental composition of cells.

6. IONpath repeatedly, and improperly, inserts the undefined phrase “individual cell event” into the plain and ordinary meaning of the limitations “detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single [first cell]/[second cell],” although IONpath nowhere explains what this newfound limitation is supposed to mean.

IONpath’s repeated attempts to rewrite the claims, insert entirely new terms and limitations, and bolt on unrelated structural requirements invites serious and reversible error that the Court should reject.

I. “VAPORIZING, ATOMIZING, AND IONIZING.”

In an effort to have the Court read *three entirely new limitations* into the claims, IONpath turns the actual language of the Patents on its head. None of its new limitations are supported by the claims, specification, or the law.

A. There is No “Three-Step” Requirement, Much Less a Required Order of Steps.

In arguing that the Patents require that “vaporization, atomization, and ionization” be defined to require that each of the three words occur “sequentially and separately,” at different times, IONpath misleadingly seizes on language in the Patents’ specification that “[i]n some

^{1/} IONpath conveniently omits with ellipses (...) and wholly misconstrues the plain language in the claim limiting detection to the transient signals of the elemental tags. *Compare, e.g.*, Ip. Br. at 16:1-3 (“This is clear from the structure of the claim itself, which recites (1) ‘vaporizing, atomizing, and ionizing . . . tags from a single first cell,’ (2) then ‘**detecting . . . the first cell,**’ ...” (emphasis added)), *with* ‘386 Patent, 30:66-31:2 (“**detecting, using mass spectrometry, the elemental composition of the first cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the first cell**”) (emphasis added).

1 instances, vaporization, atomization, and ionization ... can occur in different devices and at
 2 different times.”^{2/} Ip. Br. at 4:3-8; ‘386 Patent, 13:7-11. First, this passage alone defeats
 3 IONpath’s construction as the lead-in phrase “[i]n some instances” necessarily and implicitly
 4 means that “vaporization, atomization, and ionization” may occur *both* at the same time, in some
 5 instances, and at different times, in other instances. ‘386 Patent, 13:7 (emphasis added). Second,
 6 as Dr. Kelly explains, “vaporization, atomization, and ionization” may occur simultaneously in
 7 devices known to POSIA and taught by the Patents. *See* Kelly Rep. (ECF No. 109-2) ¶¶ 86-87.
 8 For example, in glow discharge mass spectrometry, which is expressly disclosed as a “suitable
 9 device[]” to “vaporize, atomize, and ionize” in the Patents, vaporization and atomization occur
 10 simultaneously via sputtering (just as with secondary ion mass spectrometry (“SIMS”)). *See id.*
 11 ¶¶ 87, 28-32. Third, the Patents themselves explicitly define “vaporizing, atomizing, and
 12 ionizing” as not always requiring atomization – thus, IONpath’s proposed “three-step” sequence
 13 is necessarily incorrect:

14 “the term ‘means to vaporize, atomize, and excite or ionize’ includes means where
 15 atomization may not be necessary, so that the term may or may not encompass vaporization
 followed by ionization directly.”

16 ‘386 Patent, 3:3-7.

17 Attempting to circumvent these facts, IONpath leans on a description that, in an
 18 embodiment employing one of many types of disclosed devices (ICP), “the sample is *promptly*
 19 vaporized, atomized, and ionized *as it flows through the plasma.*” Ip. Br. at 4:2-3 (quoting ‘386
 20 Patent, 13:30-32) (emphasis added). Yet, even this passage fails to contain any “stepped”
 21 language, nor does it contradict the fact that “vaporization, atomization, and ionization” may
 22 occur simultaneously. Indeed, the phrase only provides that, in this embodiment, the “vaporize,
 23 atomize, and ionize” step is performed “promptly.” If anything, the word “promptly” suggests
 24 that the “vaporize, atomize, and ionize” can occur at the same time or simultaneously such that
 25 any sequential requirement would be entirely pointless.

26
 27 ^{2/} It is worth noting that in this instance, IONpath concedes that it understands that the
 28 meaning of “sequentially” is “at different times.” Yet, in trying to read “timing” out of the claim
 term “sequentially,” with respect to detecting, IONpath eviscerates the actual meaning of the
 word from its proposed definition. Ip. Br. at 19:10-14.

With no intrinsic support for its addition of a “three-step” requirement, IONpath opts to make a conclusory proclamation that because the patent explains that a sample “flows through” plasma in the ICP embodiment, “flowing through” somehow dictates a “three-step” process. *Id.* at 4:3-4. It does not.^{3/} Rebuttal Report of Thomas Kelly (“Kelly Reb.”) ¶ 16. Nowhere do the Patents teach or require IONpath’s “three-step” process. The fact that IONpath repeatedly says that “vaporizing, atomizing, and ionizing” is a sequential process does not make it so. Indeed, the inventors knew how to use the word “sequential” -- it appears twice in Claim 1 of both Patents. But the inventors did not use the word sequential to limit “vaporizing, atomizing, and ionizing.”

The law strongly counsels against IONpath’s new, three-step, sequential limitation. As IONpath frankly admits, “it is true that claims that do not ‘explicitly recite or implicitly require’ ordering should not be construed as such.” *Ip. Br.* at 5:6-8 (quoting *Koninklijke Philips N.V. v. Zoll Med. Corp.*, 656 F. App’x 504, 514 (Fed. Cir. 2016)). IONpath is correct. The Federal Circuit has repeatedly cautioned: “Unless the steps of a method actually recite an order, the steps are not ordinarily construed to require one.” *Altiris, Inc. v. Symantec Corp.*, 318 F.3d 1363, 1369 (Fed. Cir. 2003) (quoting *Interactive Gift Exp., Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1342-43 (Fed. Cir. 2001)). To determine whether “the steps of a method claim that do not otherwise recite an order, must nonetheless be performed in the order written” a two-part test is employed. *Altiris*, 318 F.3d at 1369-70. A court looks first “to the claim language to determine if, as a matter of logic or grammar, they must be performed in the order written.” *Id.* at 1369. If the claim language does not necessitate the imposition of the written order, courts then “look to the rest of the specification to determine whether *it* ‘directly or implicitly requires such a narrow construction.’” *Id.* at 1370 (emphasis in original) (quoting *Interactive Gift*, 256 F.3d at 1343); *see also Maxim Integrated Prod., Inc. v. Silicon Mitus Tech., Inc.*, No. 17-CV-03507 NC, 2018 WL 4657384, at *7 (N.D. Cal. July 3, 2018) (employing the *Altiris* two-part test). Neither part of the *Altiris* test is

^{3/} IONpath’s expert witness’s contention that there may be, in some circumstances, nanoseconds or microseconds between phases (vaporization, atomization, and ionization) when a sample is placed in a plasma, even if true, does not equate to or require separate limitations and steps. The device or step is “vaporizing, atomizing, and ionizing” – whether by using glow discharge, SIMS, ICP, CCP, or a graphite furnace, and regardless of whether it occurs promptly over the course of microseconds. *See Kelly Reb.* ¶ 16.

1 met here. The claim language does not require they be “performed in the order written” and the
 2 specifications cannot “directly or implicitly require[] such a narrow construction” as they state
 3 that “[i]n some instances, vaporization, atomization” may occur at the same time and explicitly
 4 state that, in some embodiments, “atomization may not be necessary, so that the term may or may
 5 not encompass vaporization followed by ionization directly.” The Court should reject IONpath’s
 6 “narrow construction” as an improper importation of new limitations.

7 In asking the Court to impose a non-existent “order” of steps, IONpath is only left to
 8 vaguely assert that its expert witness opines that a POSIA would understand that stringing three
 9 words together, what it refers to as “this particular phrasing,” requires a sequence. Ip. Br. at 5:12-
 10 16. As there is no legitimate support for this argument other than its expert’s *ipse dixit*, IONpath
 11 seeks to buttress the contention by circularly contending, again, that because the word “promptly”
 12 is used with “vaporized, atomized, and ionized” in the specification, “promptly” somehow
 13 transforms the phrase into three-steps. *Id.* at 5:16-20. There is no support or basis for IONpath’s
 14 new “three-step” limitation and it should be rejected.

15 Finally, IONpath’s hyperbolic argument that Fluidigm’s proposed construction “writ[es]
 16 vaporization out of the claim” and “would require ionizing and atomizing to also be stricken”
 17 badly misconstrues the construction and the Patents. Ip. Br. at 4:18-20, 8:4-8. Fluidigm’s
 18 construction need not include the word “vaporize” for it to cover “vaporization.” Fluidigm’s
 19 construction accurately provides that the ionized atomic components are generated from a solid or
 20 liquid sample, which a POSIA understands involves vaporization. Kelly Reb. ¶ 18. IONpath’s
 21 add-on argument that because *some* glow discharge devices may not atomize, “ionizing and
 22 atomizing” are required to be stricken, is nonsensical. IONpath’s expert’s admission that “a
 23 PHOSITA **would have known** some glow discharge devices **do not require heating to vaporize a**
 24 **sample** prior to ionizing in the glow discharge device” alone concedes that glow discharge
 25 devices are capable of performing vaporization. Declaration of Nicholas Winograd, Ph.D.
 26 Regarding Claim Construction (ECF No. 113-11) (“Winograd Dec.”) ¶ 177 (emphasis added).
 27 That Dr. Winograd identified a few isolated examples of glow discharge devices with add-on
 28 sample introduction devices that involve heat does not take away from the fact that the

specification describes glow discharge (as opposed to glow discharge plus a sample introduction device) as a “suitable device” for “vaporizing, atomizing, and ionizing.” None of IONpath’s arguments are sufficient to overcome the plain language of the specification that glow discharge is an appropriate means to vaporize, atomize, and ionize.

B. Neither the Claims Nor Patents Require “Heat.”

Although “heat” is neither a limitation in the claims nor a required element to “vaporize, atomize, and ionize,” IONpath insists that the Court read “heat” into the claims. Not only is “heat” not supported by the intrinsic evidence, it directly contradicts IONpath’s effort to add the limitation. As set forth in Fluidigm’s opening Claim Construction Brief (ECF No. 109) (“Fl. Br.”), the Patents identify numerous “suitable devices” that may be used to “vaporize, atomize, and ionize” including, among others, glow discharge. Fl. Br. at 6:10-28. Glow discharge devices, just like the ion beam utilized in SIMS (the technique IONpath’s accused products employ) and other techniques such as field evaporation (used in atom probe tomography), do not employ thermal evaporation (a change in temperature, *i.e.* “heat”) to achieve vaporization. Kelly Rep. ¶¶ 77-78; Kelly Reb. ¶ 10. As such, the Patents expressly teach suitable vaporization techniques that do not require heat. Kelly Rep. ¶ 77; Kelly Reb. ¶¶ 10, 13.

In its zeal to avoid the disclosure of the use of glow discharge in the Patents, which does not employ “heat” to achieve vaporization, IONpath’s brief first mischaracterizes the technique as “heat-based.” Ip. Br at 7:7-8. Yet, just two paragraphs later, IONpath contradicts itself conceding that “there are *some* glow discharge devices that do not use heat.” *Id.* at 7:19-21 (emphasis in original). IONpath’s admission alone, that some glow discharge devices do not use heat, fully undercuts its argument that “heat” must be imported into the claims and that the Patents only teach heat-based techniques.^{4/5/} And, Dr. Kelly confirms that POSIA understand glow discharge,

^{4/} Further undermining IONpath’s argument is the fact that, as Dr. Kelly explains, POSIA understood that when glow discharge mass spectrometry is employed there is sometimes a risk that the sample temperature may increase as a result of having hot plasma nearby (the source of sputtering ions). Accordingly, POSIA often hold samples at cryogenic temperatures to specifically avoid thermal changes. Kelly Reb. ¶ 13.

^{5/} POSIA understood that while an increase in temperature may serve to accelerate vaporization, it is simply not a required component to vaporize. Kelly Reb. ¶ 10.

1 including as taught in the Patents, does not require heat. Kelly Rep. ¶ 77; Kelly Reb. ¶¶ 10-13.

2 The only intrinsic evidence IONpath points to in support of its position is an inapplicable
3 prior art reference cited in both Patents where glow discharge was used to ionize particles after
4 they were already thermally vaporized with a sample introduction device. Ip. Br. at 7:21-27
5 (citing Ex. 5 at [035]). The reference has nothing to do with the Patents' identification of glow
6 discharge devices to "vaporize, atomize, and ionize." The glow discharge device in the reference
7 was used in a different manner, did not vaporize, did not use heat, and is not even an embodiment
8 disclosed in the Patents. IONpath's argument that the Court should import a limitation from an
9 inapplicable prior art reference is not grounded in any facts or the law. The prior art reference
10 does not come close to meeting the "exacting" standard for an alleged disavowal. It would be
11 completely improper to import a limitation from a "prior art reference" "absent a clear indication
12 in the intrinsic record that the patentee intended the claims to be so limited." *GE Lighting Sols.,*
13 *LLC v. AgiLight, Inc.*, 750 F.3d 1304, 1309 (Fed. Cir. 2014); *see also id.* ("[D]isavowal requires
14 that 'the specification [or prosecution history] make[] clear that the invention does not include a
15 particular feature.'" (first alteration added) (quoting *SciMed Life Sys. Inc. v. Advanced*
16 *Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001))).

17 IONpath also attempts to disregard (in a footnote) Fluidigm's evidence that the term
18 "vaporize" is used by POSIA to refer to a variety of techniques, many of which do not use heat.
19 Ip. Br. at 6 n.5; *but see* Kelly Rep. ¶ 73. Importantly, IONpath cannot refute the fact that among
20 such techniques known to POSIA at the time was SIMS, which IONpath claims does not use heat.
21 *See* Fl. Br., Ex. K (ECF No. 109-14) at 3704 ("the vaporization process produced by many mass
22 spectrometry techniques including time-of-flight secondary ion mass spectrometry (ToF-SIMS)
23 ..."); *see also* Kelly Rep. ¶ 79.

24 "Heating" is not a required component of the claimed inventions as evidenced by, among
25 other things, the specifications identification of a glow discharge device as a suitable means to
26 "vaporize, atomize, and ionize." By IONpath's own admission, the identification of glow
27 discharge devices in both Patent specifications fully supports the fact that heat is not a required
28 element. Allowing IONpath to import such a limitation would improperly limit the clear scope of

the plain language of the claims. *See GE Lighting* at 1308 (“Nothing in the intrinsic record requires a departure from this plain and ordinary meaning.”).

II. “DETECTION” OF THE TRANSIENT SIGNALS OF THE ELEMENTAL TAGS.

IONpath’s proposed construction of the “detecting” limitations fares no better, and misleadingly ignores the plain language of the claims. The claims unmistakably lay out that it is the elemental tags that are being detected that are indirectly attached to cells, not the entire composition of the underlying cells as IONpath erroneously asks the Court to conclude. A simple reading of Claim 1 of both patents precisely describes/claims what is being detected – below is a succinct summary:

1. Cells (first and second) are tagged with multiple antibodies, where each antibody is specific to a different analyte of interest on or in the cell;

2. Wherein each antibody is also tagged with an elemental tag comprising a lanthanide or noble metal;

3. The multiple lanthanide or noble metal tags are “vaporized, atomized, and ionized,” resulting in transient signals associated with the multiple elemental tags; and

4. The signals of the multiple ionized lanthanide or noble metal tags associated with the first and second cells are detected by mass spectrometry.

Claim 1, ‘386 Patent, 30:55-31:12; Claim 1, ‘698 Patent, 30:53-31:9. IONpath is correct that it is Fluidigm’s position that the claims are clear and that no construction is necessary. Contrary to IONpath’s argument, Fluidigm is not seeking to “chop” anything up. Rather, its position is that any POSIA would understand the subject terms and limitations without construction.

IONpath, however, turns the claim language on its head and asserts that the entire claim passages that encompass the “detect” terms must be construed to require that the *entire* composition of the “first cell” and *entire* composition of the “second cell” be detected (not the “elemental tags” attached to the antibodies attached to the analytes of interest, as recited in the claims). *Ip. Br.* at 15-16 (emphasis in original). This is flatly wrong, directly contradicts the express language of the claims, and is not how a POSIA would understand the limitations. To put IONpath’s argument in context, the number of atoms in a single human cell is, approximately, 100 Trillion. *Kelly Reb.* ¶ 32. And even if this volume of cells could be handled (it can’t), practical limitations would prevent each atom from being detected (not every tag is ionized, not

every ionized tag travels to and/or makes it to the detector). *See* Kelly Rep. ¶ 111; Kelly Reb. ¶ 33. The claim language unmistakable provides that only multiple ionized lanthanide or noble metal tags associated with the analytes of interest in the first and second cells are detected by mass spectrometry – not the entire compositions of the underlying cells as IONpath disingenuously advocates. Claim 1, ‘386 Patent, 30:55-31:12; Claim 1, ‘698 Patent, 30:53-31:9.

Remarkably, in lieu of reciting the pertinent claim language in its brief, which directly contradicts its argument, IONpath opts to use ellipses excluding the operative language. IONpath would have the Court believe that the claims require “detecting ... the first cell” and “detecting ... the second cell” instead of what actually appears in the claims:

Claim 1 of the ‘386 Patent

“detecting, using mass spectrometry, the elemental composition of the first cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the first cell”

...

“detecting, using mass spectrometry, the elemental composition of the second cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the second cell”

Claim 1 of the ‘698 Patent

“to detect, by mass spectrometry, lanthanides and/or noble metals of the single first cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single first cell, and lanthanides and/or noble metals of the single second cell by detecting a transient signal of the multiple vaporized, atomized, and ionized elemental tags of the single second cell”

‘386 Patent, 30:66-31:9; ‘698 Patent, 30:66-31:6 (emphasis added). A fair reading of the claims belies IONpath’s argument that the claims require that the *entire* composition of the first and second cells be detected. The claims require only the detection of a transient signal of the multiple vaporized, atomized, and ionized elemental tags associated with the antibodies attached to the analytes of interest. Kelly Rep. ¶¶ 108-109. The fact that the detection of the ionized elemental tags is performed, cell by cell (as IONpath argues), changes nothing, and certainly does not transform the claims to require that trillions of atoms -- the *entire* elemental compositions of the cells -- be detected. No other reading is reasonable.

Finally, IONpath’s contention that there is some sort of prosecution estoppel or disclaimer

holds no water. Ip, Br. at 17-18. The amendment that IONpath relies upon simply replaced the respective instances of “single cell” with “first cell” and “second cell.” Ip. Br., Ex. 3 at 17. The amendment did not alter, in any way or form, that the only signals detected were those of the “transient signal of the multiple vaporized, atomized, and ionized elemental tags.” While the ionized elemental tags of the lanthanides and noble metals are detected, on a single cell basis, this does not translate to the detection of the *entire* composition of each cell as IONpath insists.

III. “LANTHANIDE OR NOBLE METAL.”

As IONpath admits, the parties’ dispute over these terms is minor. *See* Ip. Br. at 23. The dispute concerns whether indium, nickel, and copper fall within the definition of noble metals. The appropriate metric is not, as IONpath argues, simply whether a noble metal is “an element that resists oxidation,” (*id.*), but whether the element’s “electrochemical potential ... is much more positive than the potential of the standard hydrogen electrode, [and] therefore, ... [it] resists oxidation.” Neither IONpath nor Dr. Winograd appear to contest that “copper has an electrochemical potential that is much lower than the noble metals palladium, silver, iridium, platinum and gold that are referred to in the intrinsic record.” Kelly Rep. ¶ 140. Instead, they argue that copper should be considered a noble metal because it “has an electrochemical potential greater than the standard hydrogen electrode, and it does not readily oxidize in air.” Winograd Dec. ¶ 283. But copper does oxidize in air, as a result of having a much lower electrochemical potential than the other metals that clearly fall in the noble metal category. Kelly Reb. ¶ 43. To the extent there is any ambiguity, the fact that copper is endogenously present in biological samples resolves the issue. IONpath cannot dispute this fact and recognizes that the Patents’ specifications teach away from the use of such materials. *See, e.g.*, ‘386 Patent, 10:5-9 (“there are ... at least 35 isotopes of the lanthanides and noble metals alone that ... are not[]expected to be common in biological systems ...”).

IONpath’s other objection to Fluidigm’s construction misses the mark. Fluidigm’s construction is consistent with the agreed-upon construction of “element[al] tag” as in the context of the claims (e.g., “an elemental tag comprising a lanthanide or noble metal”), a tag refers to an “element or an isotope of *an element*,” not of an “element, isotope, ion, and/or composition.”

1 **IV. IONPATH SEEKS TO ADD AN ENTIRELY NEW PIECE OF EQUIPMENT TO “FIRST DEVICE.”**

2 Fluidigm’s and IONpath’s claim construction briefs adequately address whether the
3 claimed “first device to vaporize, atomize, and ionize multiple elemental tags ...” is governed by
4 § 112(6). Accordingly, Fluidigm will focus its Reply on this term to address, if *arguendo* the
5 Court finds § 112(6) to apply, IONpath’s arguments regarding what corresponding structure is
6 disclosed in the specification.

7 As Fluidigm’s opening brief details, the ‘698 Patent expressly identifies that the “first
8 device to vaporize, atomize and ionize multiple elemental tags” of Claim 1 includes at least the
9 following instruments: glow discharge, graphite furnace, capacitively coupled plasma, inductively
10 coupled plasma, other suitable devices, and equivalents thereof.^{6/} ‘698 Patent, 13:2-11.
11 Remarkably, in lieu of addressing the apparatuses and equivalents that comprise the “first device”
12 disclosed in the ‘698 Patent, IONpath opts to argue that a completely *unclaimed additional piece*
13 *of equipment* must be added to the claimed “first device.” Ip. Br. at 8:15-20. Specifically,
14 IONpath tries to persuade the Court that it should add “*a cell or particle injection system,*” and
15 more specifically, “*a sheath flow injection system*” to the claim. Needless to say, adding a
16 completely new and separate device to the claim, that does not even perform what IONpath
17 argues is the recited function of the claimed device (“to vaporize, atomize, and ionize multiple
18 elemental tags”) would constitute error.^{7/}

19 While IONpath admits that the claimed “first device to vaporize, atomize, and ionize
20 multiple elemental tags” does not recite, much less include, a “sheath flow injection system,” it
21 nevertheless advocates saddling its proposed claim construction with the unclaimed equipment
22 based solely upon its self-serving conclusion that a “sheath flow injection system” is necessary to
23 enable “sequential analysis of cells.” *Id.* at 12:2-15. Setting aside the fallacy of IONpath’s
24

25 ^{6/} As Dr. Kelly explains in his initial Report, equivalents “necessarily includes ... microwave
26 induced plasma, DC-glow discharge, RF-glow discharge, spark source, laser ablation/ionization,
27 ion-beam (including, but not limited to, SIMS), electrospray, capacitive microwave plasma, and
direct current plasma.” Kelly Rep. ¶ 96.

28 ^{7/} The inventors plainly knew how to claim injection systems, yet chose not to include the
apparatus in Claim 1 of the ‘698 Patent. *See, e.g.,* Ex. A (U.S. Patent App. No. 12/521,272 (“Cell
Injector for Flow Cytometer ...”)).

enablement contention, sequential analysis is not even a limitation in the “first device to vaporize, atomize, and ionize.” ‘698 Patent, 30:62-65; *see also* Kelly Rep. ¶ 98.^{8/} Further, while IONpath may wish to raise enablement as a validity defense, it is not germane to claim construction. Of course, IONpath’s motive for seeking to improperly add equipment to the claims is not a secret, it wishes to find a way to avoid its infringement. Yet, the fact that IONpath’s infringing MIBI System does not require a “sheath flow injection system” itself defeats its enablement argument.

There is simply no justification to import an unrelated and unclaimed apparatus from a disclosed embodiment into the claimed “first device to vaporize, atomize, and ionize multiple elemental tags.”

V. THE CLAIMED “SECOND DEVICE” IS A MASS SPECTROMETER.

Claim 1 of the ‘698 Patent recites “a second device to detect, by mass spectrometry, lanthanides and/or noble metals . . .” ‘698 Patent, 30:66-67. There is no ambiguity, and this dispute merits few words. The plain and ordinary meaning of the recited “second device to detect” is a “mass spectrometer” – *exactly* as recited and laid out in the claim.

Claim 1 expressly identifies that the second device detects the “lanthanides and/or noble metals” of a single cell by detecting the “transient signal of the multiple vaporized, atomized, and ionized elemental tags” of the first and second cells “by mass spectrometry” – *i.e. using a mass spectrometer*. ‘698 Patent, 30:66-31:6. No further structure need be disclosed. Any POSIA and layman would understand, as confirmed by Dr. Kelly, that expressly identifying in the claim itself that the second device detects using “mass spectrometry” means that the device is a “mass spectrometer.” Kelly Rep. ¶ 99. And even IONpath admits that the intrinsic evidence is clear that “the mass spectrometer can be any mass spectrometer.” Ip. Br. at 14:19-21 (quoting ‘698 Patent, 7:15-20).

Yet, consistent in its approach of seeking to improperly narrow the claims to avoid infringement, IONpath puts its head in the sand and argues that Claim 1 is so indefinite and provides insufficient structure for a POSIA to understand that the claimed “second device” that

^{8/} While the ‘698 Patent explains that sheath flow injection systems is one piece of equipment that may be used with one identified embodiment, ICP, it also explains that other types of equipment may be used. ‘698 Patent, 11:50-65.

performs “mass spectrometry” is a “mass spectrometer.” Ip. Br. at 14:6-8. Frankly, this is an instance where IONpath has chosen advocacy over reality. Claim 1 of the ‘698 Patent conspicuously identifies that the second device is a mass spectrometer which is entirely consistent with the specification. The limitation is not subject to § 112(6).

VI. “SEQUENTIALLY.”

At the outset, contrary to IONpath’s statement, Fluidigm does not agree and has not conceded that the preamble is limiting. Fluidigm has consistently taken the position that the preambles of Claim 1 of both Patents are not limiting as both Patents contain detailed and sufficient structure and steps such that the preambles add nothing to the claims. *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1373-74 (Fed. Cir. 2001) (“If the body of the claim sets out the complete invention, and the preamble is not necessary to give ‘life, meaning and vitality’ to the claim, ‘then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation.’”). Fluidigm has, however, properly advanced constructions in the unlikely event the Court finds either or both preambles limiting.

IONpath’s construction of the “sequentially” terms is divorced from the fundamental, and well understood, meaning of the word – as well as its own understanding. “Sequentially” indisputably has a timing aspect, that is, it means that something is performed or occurs at separate times. As discussed earlier (Section I.A.), IONpath conceded and had no difficulty understanding that “sequentially” means “at different times” when it seized upon the concept in arguing for a construction of “vaporization, atomization, and ionization.” Ip. Br. at 4:4-8. Yet, just fifteen pages later in its brief, IONpath acquires some form of amnesia and advocates a different construction. Its rationale is transparent.

IONpaths’s proposed construction of “detected sequentially” (last two words in both Claim 1 of the ‘386 and ‘698 Patents), and the preambles (“A method of sequentially analyzing single cells by mass spectrometry” [Claim 1, ‘386 Patent], and “A system for sequentially analyzing single cells in a sample by mass spectrometry” [Claim 1, ‘698 Patent]) is devoid of any timing element:

Individually discerning elemental composition on a cell-by-cell basis.

Fluidigm's construction, on the other hand, simply and properly interprets "sequentially" as used to mean "at separate times":

Detected sequentially: "observed at separate times"

Sequentially analyzing single cells: "analyzing single cells at separate times"

... in a sample: "analyzing single cells in a sample separately, not at the same time"

IONpath's complete disregard for the word "sequential" in its construction arises from its overwhelming objective to advance its non-infringement theory that the claims require the analysis of entire cells. Of course, IONpath's non-infringement theory does not provide a basis to ignore and rewrite claim terms. And, as addressed above, IONpath's theory runs completely afoul of the express language of the claims which provide that what is "detected sequentially" are the transient signals of the multiple vaporized, atomized, and ionized elemental tags that were indirectly attached (tagged) to analytes in or on the first and second cells – not the entire cells as IONpath seeks to read into the limitations. *See supra* Section II.

IONpath's request that the Court construe "sequentially" to require "discerning elemental composition on a cell-by-cell basis" has no basis in fact, is divorced from the plain meaning of the claim terms and limitations, and should be rejected.

VII. "TRANSIENT SIGNAL."

Here, again, IONpath continues its crusade to alter and read new limitations into the plain language of the claims. The claims consistently provide that the "transient signal" is that of the "multiple vaporized, atomized, and ionized elemental tags." '386 Patent, 31:6-11; '698 Patent, 31:1-6. The elemental tags, the source of the transient signals, as detailed in the claims and explained above, are comprised of lanthanide and noble metals tagged antibodies specific to analytes of interest in and on cells – not an "entire cell," nor an entire "single cell system," as IONpath insists. Simply put, elemental tags are attached to only a small fraction of atoms in or on a cell -- not every one of the 100 Trillion or so atoms in or on a cell. Kelly Reb. ¶ 41.

IONpath's construction is unrecognizable from that which is claimed and taught by the Patents. IONpath asks the Court to require that the "transient signal" be that of an entire "cell system" – not the claimed transient signals of multiple elemental tags that are attached to a cell as

1 claimed. Ip. Br. at 22:19. Tellingly, IONpath’s fallacious construction is designed to require the
 2 claimed method and system detect a “a transient of the *single cell* system.” *Id.* (emphasis in
 3 original). This is not what is claimed, taught, or described anywhere in the claims or intrinsic
 4 record. All of the intrinsic evidence is consistent. The claimed “transient signal” is the signal
 5 generated for a limited duration of time from vaporized, atomized, and ionized “elemental tags”
 6 that were connected to “a cell” – not an entire cell or cell system as IONpath advocates.

7 In advancing its flawed construction, IONpath errs by conflating its new “cell event”/
 8 “single cell system” limitation with the fact that the claimed elemental tags are associated with
 9 the analysis of specific analytes on single cells to which the elemental tags were affixed, not a
 10 “cell event” or “single cell system.” This is precisely what Dr. Kelly explained in his initial
 11 Report. Kelly Rep. ¶¶ 128-129. IONpath’s contortion of Dr. Kelly’s opinion does not change
 12 this fact. Dr. Kelly succinctly explains that the prior art does not teach the ability to analyze
 13 “multiple elemental tags from a single cell,” and that the claims only require the detection of the
 14 ions associated with the elemental tags, not that the claims require the detection of entire cells and
 15 cell systems as IONpath contends. *Id.* IONpath’s attempt to cherry-pick the words “single cell”
 16 out of context from sentences in which the words appear does not alter Dr. Kelly’s opinion.
 17 Ip. Br. at 22:21-28; *see also* Kelly Rep. ¶¶ 127-133.

18 **VIII. “DISTINCT ISOTOPE.”**

19 IONpath’s brief concedes that it has “no dispute” with Fluidigm’s construction of “distinct
 20 isotope” as it comports with what IONpath believes to be the plain and ordinary meaning of the
 21 term. Ip. Br. at 25:4. As such, the Court should adopt Fluidigm’s proposed construction.

22 **IX. “PRETREATING”**

23 IONpath admits that the only dispute between the parties as to the construction of
 24 “pretreating ...” is Fluidigm’s suggested addition of “... and transporting to the mass
 25 spectrometer.” Ip. Br. at 25:12-13. As discussed in Dr. Kelly’s report, Fluidigm’s proposed
 26 construction is consistent with the specification. Kelly Rep. ¶¶ 148-150. At a minimum, the
 27 Court should adopt the undisputed portion of Fluidigm’s proposed construction.
 28

1 Dated: August 6, 2020

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CERTIFICATE OF SERVICE

I hereby certify that on August 6, 2020, I electronically filed the above document with the Clerk of the Court using CM/ECF which will send electronic notification of such filing to all registered counsel.

Dated: August 6, 2020

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